

LETTER TO THE EDITOR

Adamantiades-Behçet's disease (Behçet's disease) and COVID-19

Dear Editor,

The immunopathogenesis of COVID-19 remains ill-defined.¹ Through hyperstimulation of the immune system, SARS-CoV2 may cause a multi-faceted inflammatory disease and generate immune-mediated organ damage even leading to fatal consequences.² However, it is still unclear, whether a modified course of COVID-19 occurs in patients with autoimmune and/or autoinflammatory diseases.^{3,4} Among them, Adamantiades-Behçet's disease (ABD; Behçet's disease) is a rare, multisystem, inflammatory disease characterized by variable vessel vasculitis and relapsing-remitting course, exhibiting both autoimmune and autoinflammatory signs.⁵ So far, rudimentary data on COVID-19 in ABD patients and no information about the proper management of ABD patients in the pandemic period exist.

In a telematic survey of 2789 Spanish patients, 28 had uveitis due to a systemic autoimmune disease.⁶ Among them, 12 were ABD patients; with six reporting clinical manifestations compatible with COVID-19. Moreover, among 2135 consecutive COVID-19 patients presented to the Hospital Clínic (Barcelona, Spain), four (0.19%) were co-diagnosed with ABD and three were hospitalized.⁷ In all four patients, ABD activity during the first COVID-19 symptoms was low. No patient required intensive care unit (ICU) treatment or mechanical ventilation. Further, 51 of 54 ambulatory ABD patients of the Necmettin Erbakan University Hospital (Konya, Turkey) continued their immunological treatment during the pandemic period; none of them developed COVID-19.⁸ Lastly, among 10 ABD patients of the Cerrahpasa Medical School (Istanbul, Turkey) with COVID-19, eight were hospitalized (median hospitalization length 7 days, interquartile range 5.5–10). Two patients were admitted to the ICU and a patient, not been on treatment for ABD before getting COVID-19, died.⁹ COVID-19 symptoms were mild in the nine patients who survived, and three patients reported exacerbations of their ABD-associated oral ulcers or arthralgia.

In a digital conference of the International Society for Behçet's disease, which took place on 22 January 2021, ABD experts reported on the association of ABD with COVID-19 in their countries (Table 1). With exception of the Netherlands, where ABD patients presented a significantly higher – almost twofold – COVID-19 prevalence (11.55%) than the general population (6.31%), the overall prevalence of COVID-19 in ABD

patients at 0.61% was significantly lower – 4.4-fold – than that in the general population (2.71%, $P < 0.00001$). Hospitalization due to COVID-19 symptoms was required in 33 of 168 COVID-19+ ABD patients (19.6%) and ICU in two patients (1.19%). Three ABD patients deceased with COVID-19 (1.79%).

The participants analysed the available data and the existing literature and based on the current evidence concluded on a list of measurements to be taken from ABD patients and their physicians during the COVID-19 pandemic:

- The prevalence of COVID-19 in patients with ABD is apparently lower than that in the general population. This may be due to ABD patients having been especially careful with social shielding.
- ABD appears not to be associated with a more severe COVID-19 course, although the number of reported cases is still low to be able to analyse the effects of disease subtypes, activity and medications on COVID-19 outcome.
- Treatment of ABD with low-dose prednisolone (<10 mg/day) and/or biologics (esp. TNF- α inhibitors) seems not to increase the risk for COVID-19 or induce a more severe course.
- Treatment initiation of ABD with high-dose prednisolone, cyclosporine A, methotrexate or cyclophosphamide should be carefully evaluated at the individual level, given some concern of increasing COVID-19 severity in general population. Patients that are already receiving these drugs should strictly adhere to self-protection and hygiene measurements.
- Although the effect of vaccination on ABD (and vice versa) is as yet unknown, anti-SARS-CoV2 vaccination is recommended. It may be advisable not to vaccinate during a significant flare of ABD. Benefits of being vaccinated versus risk of developing severe COVID-19 should be considered at an individual level, but in general possible risks of vaccination do not outweigh the potential dangers of COVID-19.
- Treatment with biologics in ABD appears:
 - To be compatible with SARS-CoV2 vaccination during ABD remission or low disease activity and should not be interrupted.
 - Not to compromise SARS-CoV2 vaccination. Serological confirmation of successful vaccination by ELISA may be recommended.
- National self-protection and hygiene measurements should be adhered to. Self-protection with masks is recommended even after vaccination.

Table 1 COVID-19 in ABD patients around the world

Country	Inhabitants ×10 ³	COVID-19 [†]	Prevalence %	ABD	ABD COVID-19 ⁺	Prevalence %	P [‡]	Hospital admission	ICU	Deceased	Data origin
Japan	126 500	428 804	0.34	213	1	0.47	0.79	1	0	0	Yokohama City University Hospital
Korea	51 640	88 922	0.17	14 000	0	–	–	0	0	0	Korean Society for Behçet's Disease
Iran	81 927	1 607 081	1.96	8400	60	0.71	<0.00001	16	1	1	National survey
Turkey	82 320	2 674 766	3.25	1500	12	0.80	<0.00001	6	0	0	Istanbul University Hospital
Greece	10 720	186 469	1.74	100	3	3.00	0.56	0	0	0	Laikon University Hospital, Athens
Italy	60 432	2 868 435	2.93	800	32	4.00	0.36	1	0	0	Associazione Sindrome e Malattia di Behçet e Behçet-like odv
Austria	8859	452 767	5.11	120	0	–	–	–	–	–	Innbruck University Hospital
Germany	82 931	2 426 819	2.93	836	1	0.12	<0.00001	1	1	0	Deutsches Register Morbus Adamantiades-Beçet e.V.
Netherlands	17 267	1 088 730	6.31	225	26	11.55	<0.00001	3	1	0	Erasmus MC University Medical Center and self-reported
UK	66 488	4 166 727	6.27	1325	33	2.49	<0.00001	5	0	2	London Centre
Total	589 084	15 989 520	2.71	27 519	168	0.61	<0.00001	33	2	3	

†SOURCE: Johns Hopkins University CSSE (26.02.2021) Reference: <https://coronavirus.jhu.edu/map.html>. ‡Chi-square statistic with Yates and Bonferroni corrections due to multiple comparisons (significant $P < 0.0055$).

- This consensus is based on expert opinion and literature evidence and complements the recommendations already published by other scientific societies¹⁰.

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Conflict of interest



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